## REMARKS

Claims 1-21, 24, and 26-48 are pending in the present application. Claims 5-8 and 27-46 were previously withdrawn from consideration as drawn to a non-elected invention. By virtue of this response, claims 9, 11-12, 14-21, and 48 have been amended. Accordingly, claims 1-4, 9-21, 24, 26, and 47-48 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

### *Election/Restriction*

The application contains claims 5-8 and 27-46 drawn to an invention non-elected with traverse in the response filed March 2, 2005. The Examiner contends that a complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144).

Applicants will address the cancellation of non-elected claims at such time when subject matter has been allowed. In the meantime, Applicants respectfully request that the Examiner hold this objection in abeyance.

### *Rejections Withdrawn*

Applicants acknowledge that the objections to claims 9-25, 47, and 48 as alternatively drawn to non-elected subject matter has been withdrawn.

Applicants acknowledge that the rejection of claims 1-4, 9-19, 22-26, and 47 under 35 U.S.C. § 101 for being non-statutory subject matter has been withdrawn.

Applicants acknowledge that the rejection of claims 1-3, 7, 9, 11, 15, 16, 17, 18, 19, and 22 under 35 U.S.C. 102(b) as allegedly being anticipated by Jefferson et al. (U.S. Patent No. 5,879,906, issued march 9, 1999) has been withdrawn.

***Claim Rejections under 35 U.S.C. 112, First Paragraph***

The Examiner has maintained the rejection of claims 9-21 and 48 under 35 U.S.C. 112, first paragraph, as allegedly filing to comply with the written description requirement for reasons made of record in the Office Action mailed August 1, 2005. On page 3 of the Office Action, the Examiner contends that the Applicants were not in possession of "immunomodulatory polynucleotides" in view of the disclosure of only immunostimulatory polynucleotides.

In the interest of expediting prosecution but without acquiescing to the Examiner's contention above, Applicants have amended the claims to recite "immunostimulatory sequence" instead of "immunomodulatory polynucleotides." These amendments are similar to the amendments made in the response dated January 4, 2006 which the Examiner acknowledges to have obviated the written description rejection from the previous Office Action. Support for this amendment is found throughout the specification and by the Examiner's own admission on page 3 of the Office Action.

In view of the foregoing, Applicants submit that the claims comply with the written description requirement of 35 U.S.C. § 112 and respectfully request that this rejection be withdrawn.

***Claim Rejections under 35 U.S.C. 112, First Paragraph***

Claims 1-4, 9-21, 24, 26 and 47-48 are rejected under Section 112, first paragraph for lack of enablement. On page 3 of the Office action, the Examiner alleges that the specification while being enabling for an isolated ISS consisting of SEQ ID NOs:18, 38 and 59, wherein the ISS is fully modified phosphorothioate oligonucleotide and increases IFN-gamma or IFN-alpha, and compositions comprising such and is optionally complexed with a cationic poly microsphere, is not enabled for immunomodulatory nucleic acids, immunostimulatory nucleic acid in general, and biodegradable microcarriers in general, or oligoriboxynucleotides, ISS linked to cationic by any means.

Applicants traverse this rejection of claims. To comply with the requirements of Section 112, first paragraph, a specification must adequately teach how to make and how to use the claimed invention, throughout its scope without undue experimentation. On page 3 of the Office Action, the Examiner states that she has maintained this rejection for lack of enablement based on reasons of record in the Office Action mailed 8-1-05. Applicants wish to point the Examiner's attention to the amendments that have been made in the claims to recite "immunostimulatory sequences" instead of "immunomodulatory polynucleotides." This amendment addresses many of the concerns expressed by the Examiner in the Office Action mailed 8-1-05.

On pages 3-4 of the current Office Action, the Examiner states that the Applicants reiterate the broad teachings of the specification in conjunction with assays designed to pick out among the vast claimed genus and that the issue here is make and use, and not make and test in an assay to see if you can potentially use. Applicants respectfully disagree with the Examiner's interpretation of the specification. The definition of "ISS" given on page 11 of the specification lists the number of ways to measure an immune response to an administration of one or more ISS so that one of skill in the art (or a potential infringer) can tell what kind of immune responses to look for after administering ISSs. The specification would be woefully incomplete if Applicants failed to teach what type of immune response one of skill in the art could expect upon administration of ISSs. By including such teachings, the Applicants have complied with the requirements for written description and enablement.

On page 4 of the Office Action, the Examiner has cited case law to support her contention that in areas of art "where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims." Applicants contend that the Examiner has not met her burden of establishing lack of enablement because she has not given any support for the contention that this field of immunostimulatory sequences is unpredictable. No references have been cited nor has an Examiner's affidavit been given. MPEP § 2164.04 states that the Examiner has the initial burden to establish a reasonable basis to question enablement for the claimed invention. In this case, the Examiner has not met this initial burden given that the

Applicants have taught a number of ISS in the specification and shown working examples of ISS in the Examples section of the specification.

Furthermore, in the Examples section of the specification, the Applicants have provided more than one species to support the genus claim. The Examples section of the specification gives many examples of ISS that were tested and shown to give immunostimulatory responses. Thus, the Examiner's reliance on case law where the finding of lack of enablement due to the existence of only one working example is misplaced. For example, the Examiner cites *In re Wright* 999 F.2d 1557 (Fed. Cir. 1993) on page 4 of the Office action. In *Wright*, the patentee had shown success with Prague Avian Sarcoma virus but tried to claim a generic claim to vaccines for pathogenic RNA viruses. *Id.* at 1558-1559. The patentee tried to rely on publications after the filing date to establish that one of skill in the art had success with other types of RNA viruses (e.g., HIV and SIV) other than his *single* working example. *Id.* at 1563-1564. The court rejected this argument as having no significance to what one of skill in the art would have believed at the time of filing of the application with respect to how the single working example could be extrapolated out to other types of RNA viruses and rejected the patentee's claim for generic coverage on vaccines for pathogenic RNA viruses.

The facts of the instant application are easily distinguishable over the facts the cases that the Examiner has cited because the Applicants here have provided a number of working examples of ISS. As such, cases such as *In re Soll, In re Fisher, In re Wright*, etc. are inapposite to the facts of the instant application because of the number of working examples provided in the specification.

Under Federal Circuit precedent, a "disclosure that names one species encompassed within a genus will adequately describe a claim directed to that genus only if the disclosure 'indicates that the patentee has invented species sufficient to constitute the genus.'" *In re Curtis*, 354 F.3d 1347, 1358 (Fed. Cir. 2004). Here, the Applicants have taught a number of ISS that are capable of immunostimulatory effects. MPEP § 2164.02 and existing case law have mandated that an Applicant does not have to show working examples for every single species encompassed within the

genus in order to get patent coverage for the genus claim. Applicants maintain that they have taught and shown enough working examples that are representative of the genus claim.

Furthermore, the Applicants have taught consensus sequences (e.g., SEQ ID NO:62) where certain nucleotides can be substituted for other nucleotides and still get immunostimulatory effects. As such, the specification provides not only a teaching of what type of sequences can be expected to have immunostimulatory sequences but also teaches how to assess the immunostimulatory effects. Accordingly, the specification is enabled for 1-4, 9-21, 24, 26 and 47-48.

In view of the foregoing, Applicants submit that the claims comply with the enablement requirement of 35 U.S.C. § 112 and respectfully request that this rejection be withdrawn.

***Claim Rejections under 35 U.S.C. 102(e)***

The Examiner has maintained the rejection of claims 1-3, 15-19, 26, and 48 under 35 U.S.C. 102(e) as allegedly being anticipated by Doucette-Stamm et al. (U.S. Patent No. 6,800,744 ('744 patent), issued October 5, 2004 with priority to provisional document 60/051,533 filed July 2, 1997) for reasons made of record in the Office Action mailed August 1, 2005. In this last Office Action, the Examiner stated that nucleotide residues 37-46 of SEQ ID NO: 1794 was 100% identical to SEQ ID NO: 77 of the instant application. On page 5 of the current Office Action, the Examiner states that the '744 patent teaches fragments and compositions comprising such as set forth in the last Office Action of record.

Applicants traverse this rejection and respectfully disagree with the Examiner's statement. For a reference to be anticipatory art, it must disclose in that single reference each and every limitation in the claim, either expressly or inherently. This requirement is not met in this case. The '744 patent contains 5206 sequence listings obtained by sequencing the genome of *S. pneumoniae*. The patent specification also discloses that subsets of the sequences listed in the 5206 sequence listings can be used as probes to detect the presence of *S. pneumoniae* (see, e.g., col. 17, lines 12-15). Thus, the possible combinations and permutations of short nucleotide probes within all the 5206 sequence listings are very large. Further the number of sequences listed themselves in

this patent is very large as well. Despite the large numbers of possible combination of sequences, the '744 patent application still fails to teach a specific subset within the 5206 sequences that would meet the limitations of the claims. For example, claim 1 recites a composition comprising an isolated ISS of a particular sequence pattern (SEQ ID NO: 62) and a pharmaceutically acceptable excipient. There is no explicit teaching of a specific subset of sequences in the '744 specification where there is a composition comprising an isolated sequence matching SEQ ID NO: 62 that also comprises a pharmaceutically acceptable excipient. Columns 6-7 of the '744 patent teaches the fragments of the sequences disclosed in the sequence listings are used as hybridization probes for diagnostic purposes. The claims of the instant invention are quite different from this teaching. The claims of the instant invention recite a composition comprising an isolated ISS and a pharmaceutically acceptable excipient. The '744 patent teaches hybridization probes for diagnosis, not pharmaceutical compositions. Accordingly, the '744 patent does not anticipate the claimed invention of the instant application.

In effect, the specification of the '744 patent have disclosed a huge genus comprising thousands of sequence listings obtained by sequencing the genome of *S. pneumoniae*. MPEP § 2131.02 states that "[a] genus does not always anticipate a claim to a species within the genus." In support of this notion, the Federal Circuit has stated that "[i]t is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus...There may be many species encompassed within a genus that are not disclosed by a mere disclosure of the genus." *Atofina v. Great Lakes Chemical Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006).

Here, the '744 patent discloses a genus comprising over 5000 sequences. In consonance with the Federal Circuit's ruling in *Atofina*, plucking merely one species of a 480 nucleotide sequence from a genus comprising thousands of sequences does not necessarily mean that it is a disclosure of that species. The possible combinations of the sequences and the fragments therein that can be used as probes, e.g., for diagnosis of *S. pneumoniae* infection, are too large to constitute an explicit teaching of a specific sequence that would meet the claim limitations. Accordingly, the

Examiner has not met her burden of showing that the '744 patent, has disclosed every single limitation of the claims in the instant application.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw this rejection.

***Claim Rejections under 35 U.S.C. 112, Second Paragraph***

Claims 9-21 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner contends that the claims are prima facie indefinite because the term "the immunomodulatory polynucleotide" lacks antecedent basis.

Applicants have amended claims 9-21 to recite "immunostimulatory sequence" instead of "immunomodulatory polynucleotide." With this amendment, the claims now have antecedent basis. As such, this rejection is obviated by the amendment. Accordingly, Applicants respectfully request that this rejection be withdrawn.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **377882001800**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By _____

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